

AMENDMENTS TO THE CLAIMS

A clean copy of those claims that are amended is presented here. Canceled claims are indicated.

1. **(Newly amended)** A composition for controlled release of a nucleic acid, comprising:

- a. a coacervate microsphere;
- b. a nucleic acid incorporated in said coacervate microsphere; and
- c. a delivery agent incorporated in said coacervate microsphere,

wherein the coacervate microsphere comprises a polycationic molecule and a polyanionic molecule other than said nucleic acid and the delivery agent is other than said polycationic molecule of the coacervate microsphere.

2. **(Canceled)**

4. **(Newly amended)** The composition of claim 1, wherein said nucleic acid is a transfer vector.

5. The composition of claim 4, wherein said transfer vector includes a transgene.

6. The composition of claim 4, wherein said delivery agent is at least one of the following: amphiphilic molecule, lipid or polylysine.

7. **(Newly amended)** The composition of claim 1, wherein said microsphere is crosslinked by a crosslinking agent.

8. **(Previously amended)** The composition of claim 7, wherein said crosslinking agent comprises a metal cation.

9. The composition of claim 8, wherein said metal cation comprises calcium.

10. **(Newly amended)** The composition of claim 1, wherein said polyanionic molecule is alginate.

11. **(Newly amended)** The composition of claim 1, wherein said polycationic molecule is gelatin.

12. **(Newly amended)** The composition of claim 1, wherein said polycationic molecule is gelatin, and wherein said polyanionic molecule is alginate.

13. The composition of claim 4, wherein said transfer vector comprises at least one regulatory element.

14. The composition of claim 13, wherein said regulatory element is a promoter.

15. The composition of claim 4, wherein said transfer vector comprises an expression vector.

16. The composition of claim 4, wherein said transfer vector comprises a viral vector, said delivery agent is a virus, and said virus comprises at least about five percent by weight of said microsphere.

17. **(Newly amended)** The composition of claim 15, wherein said microsphere, when administered to a host, provides controlled release of said expression vector.

18. **(Newly amended)** The composition of claim 17, wherein said delivery agent facilitates intracellular delivery of said expression vector in said host.

19. **(Newly amended)** The composition of claim 18, wherein said expression vector produces a recombinant protein in said host.

20. **(Canceled)**

21. The composition of claim 4, wherein said microsphere is lyophilized.

22. The composition of claim 17, wherein said microsphere further comprises a second expression vector.

23. The composition of claim 1, wherein said nucleic acid is a viral vector, and said delivery agent is a virus.

24. **(Newly amended)** The composition of claim 1, wherein said delivery agent is a virus of said a viral vector.

25. The composition of claim 24, wherein said viral vector contains a transgene.

26. **(Previously amended)** The composition of claim 24, wherein said viral vector contains a nucleic acid encoding a recombinant gene product.

27. **(Canceled)**

28. The composition of claim 24, wherein said viral vector and said virus of said viral vector are one of the following: recombinant retrovirus, adenovirus, adeno-associated virus, or herpes simplex virus-1.

29. **(Newly amended)** A gene delivery system for transducing cells, comprising: a coacervate microsphere encapsulating at least a nucleic acid and a delivery agent that is other than a polycation of the coacervate microsphere, for facilitating intracellular delivery of said nucleic acid, wherein upon contact of cells with said coacervate microsphere, controlled release of said nucleic acid results in transduction of the cells by said nucleic acid.

30. **(Newly amended)** A method for delivering a nucleic acid into a cell, comprising: contacting a cell with a composition comprising a coacervate microsphere, wherein:

i. said coacervate microsphere incorporates a nucleic acid contained in a transfer vector having at least one regulatory element;

ii. said coacervate microsphere comprises a polycationic molecule and a polyanionic molecule other than said nucleic acid; and,

iii. said coacervate microsphere incorporates a delivery agent,

wherein said contacting of a cell with said composition results in controlled release of said transfer vector in the cell.

31. The method of claim 30, wherein said transfer vector is a viral vector, said delivery agent is a virus of said viral vector, and said viral vector is enveloped in said virus.

32. **(Newly amended)** The method of claim 31, wherein the nucleic acid encodes a bioactive protein, the cell is in a host and is transfected with the nucleic acid and expresses the bioactive protein.

33. The method of claim 31, wherein said virus facilitates intracellular delivery of said viral vector.

34. **(Newly amended)** The method of claim 31, further comprising administering said coacervate microsphere as a pharmaceutical composition to a host.

35. **(Newly amended)** A kit containing a gene delivery system, comprising microspheres and instructions for using said microspheres, wherein said microspheres are comprised of a polycationic molecule and a polyanionic molecule and said microspheres encapsulate a virus.

36. A coacervate microsphere for sustained release of a virus, comprising: a coacervate of gelatin and alginate having a virus incorporated therein.

37. **(Previously amended)** The coacervate microsphere of claim 36, wherein said virus comprises a recombinant virus.

38. A method for the sustained release of a virus to a target site, comprising: providing to the target site a coacervate microsphere comprising a coacervate of gelatin and alginate having a virus incorporated therein.

39. **(Newly amended)** A method for preparing a pharmaceutical preparation, comprising combining a pharmaceutically acceptable excipient with a coacervate microsphere of polycationic and polyanionic molecules, wherein a recombinant virus is encapsulated in said coacervate microsphere.

40. **(Newly amended)** A method for preparing a gene delivery system, comprising:

a. preparing a first solution of polycationic molecules and a second solution of polyanionic molecules;

b. adding to either said first solution or said second solution a nucleic acid; and adding to either said first solution or said second solution a delivery agent;

c. combining said first solution and said second solution to form a third solution comprising the nucleic acid and the delivery agent; and,

d. isolating coacervate microspheres formed from a portion of said polycationic molecules and a portion of said polyanionic molecules from said third solution,

wherein said coacervate microspheres encapsulate at least a portion of said nucleic acid and said delivery agent.

41. **(Cancelled)**

42. **(Newly amended)** The method of claim 40, wherein said delivery agent comprises a virus particle including said nucleic acid.

43. **(Newly amended)** The method of claim 40, further comprising mixing said third solution to form said coacervate microspheres.

44. The method of claim 42, wherein said first and said second solution are substantially aqueous.

45. The method of claim 42, further comprising preparing said microspheres for administration to a host, wherein preparing said microspheres does not impair the controlled release of said virus particle from said microspheres.

46. **(Newly amended)** The method of claim 40, further comprising lyophilizing said microspheres after said isolation.

47. **(Newly amended)** A coacervate microsphere for transfection and expression of a recombinant protein prepared by the process comprising:

a. in any order:

i. adding a polycationic molecule to a first aqueous solution;

ii. adding a polyanionic molecule to a second aqueous solution; and,

iii. adding to either said first or said second solution a virus comprising a viral vector comprising a nucleic acid encoding a recombinant protein and at least one regulatory element;

b. mixing said first and second solution together to form a coacervate microsphere of said polycationic molecule and said polyanionic molecule encapsulating said virus; and,

c. isolating said coacervate microsphere.

wherein said coacervate microsphere releases said virus in vivo or in vitro, whereby said virus transfects cells, resulting in expression of said recombinant protein.

48. **(Newly amended)** A gene delivery system for transfecting a cell with a viral vector, comprising:

- a. encapsulation means for encapsulating a viral vector;
- b. delivery means for facilitating intracellular delivery of said encapsulated viral vector;

wherein said encapsulation means comprises a coacervate microsphere, and wherein release of said encapsulated viral vector from said encapsulation means transfects a cell.

49. The composition of claim 1, wherein the nucleic acid encodes a polypeptide which inhibits cell proliferation.

50. **(New)** A method for the sustained release of a virus to a cancer cell, comprising providing to the target site, a coacervate microsphere comprising a coacervate microsphere of gelatin and alginate having a virus incorporated therein.